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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
EPPERSON, JON D	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 06/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/668,778	BALINT ET AL.	
	Examiner	Art Unit	
	Jon D. Epperson	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *63-74* is/are pending in the application.

4a) Of the above claim(s) *64 and 68-70* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *63,65-67 and 71* is/are rejected.

7)☒ Claim(s) *72-74* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/18/04;9/22/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

5.00

DETAILED ACTION

Status of the Application

1. Receipt is acknowledged of a Response to a Restriction Requirement, which was dated on March 4, 2005.

Status of the Claims

2. Claims 63-74 were pending in the present application. Applicant amended claim 67. No claims were added or canceled. Therefore, claims 63-74 are currently pending.

3. Please note: Applicant's *specifically* elected species (e.g., see 3/4/05 Response, page 7) was searched and was not found in the prior art. Thus, the search was expanded to non-elected species, which *were* found in the prior art, see rejections below. Also, see MPEP § 803.02 (emphasis added):

> On the other hand, should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a nonelected species, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. ***The prior art search, however, will not be extended unnecessarily to cover all nonelected species.*** Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection, as by amending the Markush-type claim to exclude the species anticipated or rendered obvious by the prior art, the amended Markush-type claim will be reexamined. The prior art search will be extended to the extent necessary to determine patentability of the Markush-type claim. In the event prior art is found during the reexamination that anticipates or renders obvious the amended Markush-type claim, the claim will be rejected and the action made final. Amendments submitted after the final rejection further restricting the scope of the claim may be denied entry.

4. Claims 64, 68-70 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected species (see below i.e., ***Response to Restriction and/or Election of Species***).

5. Therefore, claims 63, 65-67 and 71-74 are examined on the merits in this action.

Response to Restriction and/or Election of Species

6. Applicant's election of species is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election of species has also been treated as an election without traverse (MPEP § 818.03(a) and/ or 37 CFR 1.111(b)).

7. As a result, the restriction requirement and/or election of species is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

8. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98 (b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on the form PTO-892, they have not been considered.

9. The references listed on applicant's PTO-1449 form have been considered by the Examiner. A copy of the forms are attached to this Office Action (e.g., 3/18/04 and 9/22/03).

Specification

10. The abstract of the disclosure is objected to because it contains more than 150 words. The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details. The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc. (e.g., see MPEP § 608.01).

11. The specification is objected to over several occurrences of "grant No._____" and "awarded by _____" (e.g., page 1, line 14). Applicant must amend the specification to provide the required information at all appropriate locations.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 63, 65 and 71 are rejected under 35 U.S.C. 103(a) as being unpatentable over Michnick et al. (U.S. Patent No. 6,270,964 B1) (Filing date is **February 2, 1998**) (9/22/03 IDS Ref. AB) and Blau et al. (WO 98/44350) (Date of **October 8, 1998**) (9/22/03 IDS Ref. AG) and Pieper et al. (Piper, U.; Hayakawa, K.; Li, Z., Herzberg, O. "Circularly Permuted β-lactamase from *Staphylococcus aureus* PC1" *Biochemistry* **1997**, *36*, 8767-8774) (9/22/03 IDS Ref. BI).

For ***claim 63***, Michnick et al. (see entire document) teach protein fragment complementation systems and method of use (e.g., see Michnick et al., abstract and claims; see also column 7, last paragraph), which renders Applicants' claimed invention obvious. Michnick et al. teach a genus of fragment complementation fusion polypeptides that encompasses Applicants' claimed invention (or at least overlaps in scope to a large extent). For example, Michnick et al. disclose a protein "fragment complementation" system comprising a "first fusion product" and a "second fusion product" (i.e., a system) that contains two enzyme fragments (that encompass the two currently claimed β-lactamase fragments) and also two molecular domains that are roughly equivalent in

scope to the claimed interactor domains (e.g., see Michnick et al., claim 1; see also figure 1; see also Examples). Michnick et al. also disclose the "reconstitution" of said first and second interactor domains to yield a functional enzyme (e.g., see claim 1, "wherein reassembly of the enzyme fragments ... is detected by means of reconstitution of activity of said enzyme"; see also figure 1).

For ***claim 71***, Michnick et al. also teach the use of short peptide linkers (e.g., see column 4, paragraph 1, "One particular strategy for designing a protein complementation assay (PCA) is based on ... resulting new N- and C-termini should be on the same face of the protein [e.g., enzyme] to avoid the need for long peptide linkers [i.e., short peptide linkers are preferred] and allow for studies of orientation-dependence of protein binding"; see also figure 2 and Examples wherein a short flexible polypeptide linker was used with the DHFR PCA).

The prior art teachings of Michnick et al. differ from the claimed invention as follows:

For ***claim 63***, Michnick et al. are deficient in that they do not specifically teach the use of the "Class A β-lactamase" enzyme. Michnick et al. only teach the use of enzymes "in general" (e.g., see claim 1; see also column 8, lines 18-21, "It should be understood that the instant invention is not limited to the PCAs presented here, as numerous other enzymes can be selected and used in accordance with the teachings of the present invention"; see also abstract wherein examples like murine dihydrofolate reductase (DHFR) are provided). Michnick also provide further guidance that "teaches toward" Applicants' claimed β-lactamase (e.g., see Michnick et al., paragraph bridging

columns 9-10, "In designing a protein-fragment complementation assay (PCA), we sought to identify an enzyme for which the following is true: 1) An enzyme that is relatively small and monomeric [this is true for β-lactamase], 2) for which structural and functional information exists [this is true for β-lactamase], 3) for which simple assays exist for both *in vivo* and *in vitro* measurement [this is true for β-lactamase], and 4) for which overexpression in eukaryotic and prokaryotic cells has been demonstrated [this is true for β-lactamase]").

For ***claim 65***, Michnick et al. fail to disclose a fragment complementation system wherein said first and second class A β-lactamase protein break-points are within 10 amino acids in either direction from a junction between 2 amino acid residues of a loop between elements of secondary structure.

However, the combined references of Blau et al. and Pieper et al. teach the following limitations that are deficient in Michnick et al.:

For ***claim 63***, the combined references of Blau et al. and Pieper et al. (e.g., see entire documents) teach the use of a β-lactamase in a complementation systems like the one disclosed by Michnick et al. (e.g., see Blau et al., claim 21, "providing a reporter system comprising: a first component comprising a first low affinity reporter subunit, coupled to the first putative binding moiety, and a second component comprising a second low affinity reporter subunit coupled to the second putative binding moiety"; see also page 22, first full paragraph, "In one embodiment of the invention, the reporter subunits comprise an Enzyme ... Exemplary enzymes include ... β-lactamase"; see also page 14, lines 11-18; see also page 11, lines 21-24"). In addition, the combined

references of Blau et al. and Pieper et al teach the exact point at which a "class A" β-lactamase can be cleaved to form N-terminal and C-terminal fragments and yet still retain biological activity (e.g., see Pieper et al., abstract wherein the cp254 that was "cleaved in a loop remote from the domain interface" retained "similar" activity to the wild-type β-lactamase; see also cp228 construct, which shows rates that are 0.5-1% of the native enzyme against some substrates and 10-fold faster than the wild type against a third generation cephalosporin).

For ***claim 65***, the combined teachings of Blau et al. and Pieper et al. disclose a break-point within two amino acid residues of a loop between elements of secondary structure (e.g., see Pieper et al., abstract, "The first construct, termed cp254, was cleaved in a loop remote from the domain interface"; see also figure 1; see also Materials and Methods).

For ***claim 71***, the combined teachings of Blau et al. and Pieper et al. also disclose a flexible linker between 3-30 amino acids in length (e.g., see Blau et al., pages 16-17, Linking of the Reporter Subunit and the Binding Moiety section, especially, page 16, lines 18-21; see also Pieper et al. figure 1 showing short peptide linker).

It would have been prima facie obvious to one skilled in the art at the time the invention was made to use a class A β-lactamase enzyme as taught by the combined teachings of Blau et al. and Pieper et al. with the complementation systems as disclosed by Michnick et al. because Michnick et al. teach a general methodology for producing and/or using a complementation system and the combined teachings of Blau et al. and Pieper et al. explicitly state that a β-lactamase can be used for this purpose (e.g., see Blau

et al., page 22, first full paragraph, "In one embodiment of the invention, the reporter subunits comprise an Enzyme ... Exemplary enzymes include ... β-lactamase"). Furthermore, one of ordinary skill in the art would have been motivated to use the a class A β-lactamase because Michnick et al. state, "In designing a protein-fragment complementation assay (PCA), we sought [i.e., were motivated] to identify an enzyme for which the following is true: 1) An enzyme that is relatively small and monomeric, 2) for which structural and functional information exists, 3) for which simple assays exist for both *in vivo* and *in vitro* measurement, and 4) for which overexpression in eukaryotic and prokaryotic cells has been demonstrated" (e.g., see Michnick et al., paragraph bridging columns 9-10), which are factors that all point toward the class A β-lactamase (see above). In addition, Pieper et al. demonstrate that a high degree of activity is retained upon fragmentation of the enzyme for constructs like cp254 and a range of activities for constructs like cp228 depending on the nature of the substrate (e.g., see Pieper, abstract, wherein the cp254 construct activity is disclosed as being "very similar" to the wild type; see also page 8773, column 1, Enzymatic Activity section). Finally, one of ordinary skill in the art would have reasonably expected to be successful because Blau et al. explicitly state that a β-lactamase can be used in complementation systems (e.g., see Blau et al., page 22, first full paragraph, "In one embodiment of the invention, the reporter subunits comprise an Enzyme ... Exemplary enzymes include ... β-lactamase") and Pieper et al. provide explicit examples showing that a class A β-lactamase may be "functionally reconstituted" (e.g., see Pieper et al., abstract, cp254 and cp228 constructs). In addition, Michnick et al. state, "It should be understood that the instant invention is not limited to

the PCAs presented here, as numerous other enzymes can be selected and used in accordance with the teachings of the present invention" (e.g., see also column 8, lines 18-21), which would encompass a β-lactamase.

15. Claims 63, 65, 66 and 71 are rejected under 35 U.S.C. 103(a) as being unpatentable over Michnick et al. (U.S. Patent No. 6,270,964 B1) (Filing date is **February 2, 1998**) (9/22/03 IDS Ref. AB) and Blau et al. (WO 98/44350) (Date of **October 8, 1998**) (9/22/03 IDS Ref. AG) and Pieper et al. (Piper, U.; Hayakawa, K.; Li, Z., Herzberg, O. "Circularly Permuted β-lactamase from *Staphylococcus aureus* PC1" *Biochemistry* **1997**, *36*, 8767-8774) (9/22/03 IDS Ref. BI) and Moore et al. (Moore, J. T.; Davis, S. T.; Dev, I. K. "The development of β-lactamase as a highly versatile genetic reporter for eukaryotic cells" *Analytical Biochemistry* **1997**, *247*, 203-208) and Maveyraud et al. (Maveyraud, L.; Pratt, R. F.; Samama, J.-P. "Crystal Structure of an Acylation Transition-State Analog of the TEM-1 β-Lactamase. Mechanistic Implications for Class A β-Lactamases" *Biochemistry* **1998**, *37*, 2622-2628).

For ***claims 63, 65 and 71***, the combined references of Michnick et al., Blau et al. and Pieper et al. teach all the limitations stated in the 35 U.S.C. 103(a) rejection above (incorporated in its entirety herein by reference), which renders obvious claims 63, 65 and 71.

The prior art teaching of Michnick et al., Blau et al. and Pieper et al. differ from the claimed invention as follows:

For ***claims 66***, the prior art teachings of Michnick et al., Blau et al. and Pieper et al. differ from the claimed invention by not specifically reciting the use of SEQ ID NO:2 (i.e., TEM-1 β-lactamase).

However, Moore et al. and Maveyraud et al. teach the following limitations that are deficient in Michnick et al., Blau et al. and Pieper et al.:

For ***claims 66***, the combined references of Moore et al. and Maveyraud et al. (see entire documents) teach the use of SEQ ID NO:2 (e.g., see Moore et al., abstract wherein TEM-1 β-lactamase is disclosed; see also Materials and Methods).

It would have been prima facie obvious to one skilled in the art at the time the invention was made to use SEQ ID NO:2 as taught by the combined teachings of Moore et al. and Maveyraud et al. with the complementation system as disclosed by Michnick et al., Blau et al. and Piper et al. because the combined references of Michnick et al., Blau et al. and Piper et al. explicitly state that a β-lactamase can be used for this purpose (e.g., see Blau et al., page 22, first full paragraph, "In one embodiment of the invention, the reporter subunits comprise an Enzyme ... Exemplary enzymes include ... β-lactamase"), which would encompass the β-lactamase disclosed by the combined references of Moore et al. and Maveyraud et al. Furthermore, one of ordinary skill in the art would have been motivated to use SEQ ID NO:2 because Michnick et al. state, "In designing a protein-fragment complementation assay (PCA), we sought [i.e., were motivated] to identify an enzyme for which the following is true: 1) An enzyme that is relatively small and monomeric [this is true for SEQ ID NO:2], 2) for which structural and functional information exists [this is true for SEQ ID NO:2], 3) for which simple assays exist for

both *in vivo* and *in vitro* measurement [this is true for SEQ ID NO:2], and 4) for which overexpression in eukaryotic and prokaryotic cells has been demonstrated [this is true for SEQ ID NO:2]" (e.g., see Michnick et al., paragraph bridging columns 9-10). In addition, the combined references of Moore et al. and Maveyraud et al. state that TEM-1 β-lactamase is a good reporter because is provides "background free" measurements (which is not the case for other systems like β-galactosidase) using a "variety of substrates which are efficiently cleaved" that can be "continuously monitor[ed] ... without destruction of cells" (e.g., see Moore et al., abstract). Finally, one of ordinary skill in the art would have reasonably expected to be successful because Blau et al. explicitly state that a β-lactamase can be used in complementation systems (e.g., see Blau et al., page 22, first full paragraph, "In one embodiment of the invention, the reporter subunits comprise an Enzyme ... Exemplary enzymes include ... β-lactamase") and the combined references of Moore et al. and Maveyraud et al. further state that SEQ ID NO:2 [i.e., TEM-1 β-lactamase] is "extremely versatile in that it can be fused to other proteins and retain activity" (e.g., see Moore et al., abstract), which would encompass the "fusion" polypeptides used in the complementation systems of Michnick et al., Blau et al., and Piper et al. (e.g., see Michnick et al., claim 1 and Summary of Invention).

Double Patenting

16. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686

F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. Claims 63, 65-67 and 71 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 63-65 of U.S. Patent Application No. 09/526,106 (referred to herein as '106) in view of Michnick et al. (U.S. Patent No. 6,270,964 B1) (Filing date is **February 2, 1998**) and Blau et al. (WO 98/44350) (Date of **October 8, 1998**).

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examiner application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1986).

Here, claims 63-65 of '106 recite polypeptides containing a first interactor domain, flexible polypeptide linker and an N-terminal β-lactamase fragment that fall within the scope of the first (or second) oligopeptide of the presently claimed invention that likewise contains an N-terminal fragment of a Class A β-lactamase, an interactor domain and a linker including the use of SEQ ID NO:2 and breakpoint at E197/L198 (also referred to as E172/L173 depending on the numbering convention) (e.g., compare claims 63-65 of '106 to claims 63, 65-67 and 71 of the

currently claimed invention). The present application differs from '106 by further reciting a "second" oligopeptide to form a fully functional complementation system (i.e., the "first" + the "second" oligopeptide = complementation system). However, Michnick et al. and Blau et al. et al. teach the advantage of using both a "first" and a "second" oligopeptide to form a fully functional complementation system (e.g., see Michnick et al., claim 1; see also Blau et al., claim 1). Therefore, it would have been obvious to use a "first" oligopeptide as disclosed in the '106 patent with a "second" oligopeptide as taught by the combined references of Michnick et al. and Blau et al. et al. because complementation systems require "two" polypeptides in order to be useful (e.g., see Michnick et al., Summary of Invention, see also figure; see also Blau et al., Summary of Invention). One having ordinary skill in the art would have been motivated to make such a modification because Michnick et al. and Blau et al. et al. explicitly state that such systems are useful for β-lactamase polypeptides (e.g., see Blau et al., claim 21, "providing a reporter system comprising: a first component comprising a first low affinity reporter subunit, coupled to the first putative binding moiety, and a second component comprising a second low affinity reporter subunit coupled to the second putative binding moiety"; see also page 22, first full paragraph, "In one embodiment of the invention, the reporter subunits comprise an Enzyme ... Exemplary enzymes include ... β-lactamase"; see also page 14, lines 11-18; see also page 11, lines 21-24"; see also Michnick et al., paragraph bridging columns 9-10, "In designing a protein-fragment complementation assay (PCA), we sought to identify an enzyme for which the following is true: 1) An enzyme that is relatively small and monomeric [this is true for β-lactamase], 2) for which structural and functional information exists [this is true for β-lactamase], 3) for which simple assays exist for both *in vivo* and *in vitro* measurement [this is

true for β-lactamase], and 4) for which overexpression in eukaryotic and prokaryotic cells has been demonstrated [this is true for β-lactamase]"), which would encompass the β-lactamase disclosed by '106. Furthermore, the claim 63 of '106 expressly states that the fragment is to be used in a complementation system, which would encompass the complementation systems disclosed by the combined references of Michnick et al. and Blau et al. Finally, a person of skill would have reasonably expected to be successful because Blau et al. explicitly state that a β-lactamase can be used in complementation systems that comprise two fragments (e.g., see Blau et al., page 22, first full paragraph, "In one embodiment of the invention, the reporter subunits comprise an Enzyme ... Exemplary enzymes include ... β-lactamase").

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

18. Claims 63, 65-67 and 71 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 12 and 13 (especially claim 13) of copending Application No. 10/330,811 (Pub. No.: US 2003/0175836 A1) (referred to herein as '811). Although the conflicting claims are not identical, they are not patentably distinct from each other because the examined claims are either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1986). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 63, 65-65 and 71 are generic to all that is recited in claims 13 of '811. That is, claim 13 of '811 falls entirely within

the scope of claim 63, 65-67 and 71 of the present application or, in other words, claims 63, 65-67 and 71 are anticipated by claim 13 of '811. Specifically, **[1]** '811 discloses the α197 ω198 fragments (e.g., see claim 12) that fall within the scope of the Class A β-lactamase fragments disclosed in claims 63, 65-67 and 71 of the present application, **[2]** '811 discloses first and second leucine zipper moieties that fall within the scope of a first and second interactor domain as disclosed in claims 63, 65-67 and 71 of the present application and **[3]** both application also disclose the "reconstitution" of the enzyme (e.g., compare claim 1 in both applications).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Relevant Prior Art

19. Two references by Michnick et al. (e.g., U.S. Patent No. 6,828,099 B2 and U.S. Patent Application 2004/0161787 A1) disclose Applicants' currently claimed complementation system using a β-lactamase (e.g., see '099 patent, Summary of Invention, see especially claim 3 wherein β-lactamase is claimed). However, the 09/017,412 (filed **Feb. 2, 1998**) application to which priority is claimed (for both references) fails to provide adequate written support under 35 U.S.C. § 112, first paragraph for the β-lactamase embodiment.

Allowable Subject Matter

20. Claim 72-74 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon D. Epperson, Ph.D.
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